CLINICAL CRITERIA FOR USE
RITUXIMAB IN RHEUMATOID ARTHRITIS

Indications

1. Refractory Rheumatoid Arthritis:
   - Patient who have failed treatment with ≥ 3 synthetic disease-modifying anti-rheumatic drugs (sDMARDs) taken for ≥ 6 months.
   - Patients have displayed good levels of adherence on failed regimens.

Decision to use rituximab to be made on a named-patient basis, by institutional or provincial Pharmacy and Therapeutic Committees (PTCs).

Tests/screening/monitoring

Baseline/screening tests

- Base line blood tests:
  - » Full blood count (FBC)
  - » Differential white cell count (WCC)
  - » Alanine transaminase (ALT)
  - » Urea and Electrolytes (U&E)
  - » Creatinine
  - » Serum IgG
  - » C-reactive protein (CRP)
  - » Rheumatoid factor (RF)
  - » Anti-cyclic citrullinated peptide (ACPA), also known as anti-CCP
  - » HIV status
  - » Hepatitis B surface antigen[i]
  - » Hepatitis B surface antibodies [i]
  - » Hepatitis B core antibody [i]
  - » Hepatitis C serology
- Chest X-ray
- Check vaccination status. Manage as for Asplenic patients; see Adult and Hospital Level Standard Treatment Guidelines, *Chapter 9 Systemic and Healthcare-Associated Infections, Section 9.2 Adult vaccination*s.

Monitoring

- Monitoring blood tests (3-6 monthly):
  - » Full blood count (FBC)
  - » Differential white cell count (WCC)
  - » Alanine transaminase (ALT)
  - » Urea and Electrolytes (U&E)
  - » Creatinine
  - » C-reactive protein (CRP)
  - » Serum IgG
  - » Hepatitis B surface antigen (6 monthly)
- Simplified disease activity index (SDAI)

Regimen

Medicine	Rituximab
Route	Intravenous infusion
Dose	500mg
Cycles	2 doses separated 2 weeks apart administered at day 1 and 15
Repeated	Repeated at 6 monthly intervals dependent on response

General Treatment Principles:

- Use in combination with methotrexate (MTX) and if MTX is contra-indicated, rituximab should be used alone, or with leflunomide (LEF);
- Used by specialist physicians experienced in diagnosis and treatment of RA, and as approved by the PTC;
- Patients with rheumatoid arthritis (RA) on rituximab should be assessed for response at an interval of not <16 weeks and ideally at 24 weeks. Patients who do not show at least a moderate SDAI (≥70%) response to the first treatment course should not be considered for re-treatment.
- Re-treatment with rituximab in RA should be considered when initial treatment response of at least a moderate SDAI response has been lost. The frequency of infusion should be not <24 weeks.
- Immunoglobulin levels should be checked before commencing rituximab in RA, as well as 4–6 months after infusions and before any re-treatment. It is recommended that the possibility of increased risk of infection in patients with low immunoglobulin G (IgG) <6 g/l be discussed with them before re-treatment with rituximab. Approximately 5% of patients will develop low IgG levels on at least 1 occasion, but only 1% will have sustained low levels. Of those with sustained low IgG approximately 20% will experience a serious infection.[ii]
- Immunoglobulin replacement therapy may be considered in patients with recurrent severe infections not controlled by appropriate vaccinations and prophylactic antibiotics. [iii]
- Repeat treatment with rituximab in RA should be decided on clinical grounds, not on B-cell numbers.
- Caution should be exercised when considering the use of rituximab in patients with a history of recurring or chronic infections or with underlying conditions, which may further predispose patients to serious infection.
- Patients with RA who have not already had pneumococcus immunization should ideally receive this 4–6 weeks before commencing the first course of rituximab.
- RA patients should receive influenza vaccination before rituximab treatment and annually (before rituximab re-treatment if possible) at a time when B cells are likely to be returning to normal
- Screening of risk factors for hepatitis B and C infection should be undertaken in all patients before going on to rituximab. In patients who are HBV positive, a risk/benefit assessment should be undertaken, as treatment may be safe if appropriate anti-viral treatment is given. Rituximab treatment may be safe in patients with hepatitis C, but there are reports of severe infusion reactions in up to 25% of these patients. Hepatitis serology should be monitored in patients with evidence of past or present current hepatitis B or C infection.
- No re-treatment with rituximab and prompt reduction or discontinuation of other immunosuppressants should be undertaken when progressive multifocal leucoencephanopathy is suspected, and appropriate investigations should be undertaken.
- All patients receiving rituximab intravenously should be infused as per standard protocol approved.

Registry details

All patients warranting the use of rituximab in rheumatoid arthritis and initiated on a named patient based as per above indication are to be recorded on PTC registry. The following data will be recorded: age, gender, date of diagnosis of RA, relevant comorbidities, history of sDMARD therapy, SDAI at base line and at each monitoring visit, baseline blood tests and monitoring blood tests, (see proposed registry template).

---

[i] Kusumoto S, Tobinai K. Screening for management of hepatitis B virus reactivation in patients treated with anti-B-cell therapy. American Society of Hemotology, 2014: 576 – 583.

[ii] Van Vollenhoven RF, et.al. Longterm safety of patients receiving rituximab in rheumatoid arthritis clinical trials. The Journal of Rheumatology. 2010; 37: 558-567.

[iii] Srini Kaver. Advances in treatment of primary and secondary immune deficiencies. Curr Opin Allergy Clin Immunol 2013, 13 (Supppl 2):S51-S78